

REMARKS

In the Office Action, the Examiner rejected claims 1-12 under 35 U.S.C. §112, second paragraph as being indefinite, rejected claims 1-5 under 35 U.S.C. §102(b) as being anticipated by Herlyn et al. (US 20020081711), and rejected claims 1-25 under 35 U.S.C. §102(a) as being anticipated by, or alternatively under 35 U.S.C. §103(a) as being obvious over, Zhao et al. (Proc. Natl. Acad. Sci. USA 102:1359-1368, 2003). Each rejection raised by the Examiner is addressed separately below. In view of the amendments noted above and the remarks below, applicants respectfully request reconsideration of the merits of this patent application.

No extension of time is believed to be necessary and no fee is believed to be due in connection with this response. However, if any extension of time is required in this or any subsequent response, please consider this to be a petition for the appropriate extension and a request to charge the petition fee to Deposit Account No. 17-0055. No other fee is believed to be due in connection with this response. However, if any fee is due in this or any subsequent response, please charge the fee to the same Deposit Account No. 17-0055.

Indefiniteness rejection under 35 U.S.C. §112, second paragraph

Although the Examiner stated at the beginning of the rejection that claims 1-12 are rejected as being indefinite, the details that follow indicate that claim 8 is not rejected. Clarification is respectfully requested.

The Examiner first rejected claims 1-5 as being indefinite alleging that it is not clear as to whether the 2-hydroxyethidium compound being claimed occurs in nature or is isolated by a manmade process. Applicants respectfully traverse the rejection in that claims 1-5 clearly specify that the 2-hydroxyethidium compound being claimed is "substantially purified 2-hydroxyethidium," which is defined in the specification as "a 2-hydroxyethidium-containing composition at least 80% (by weight) of which (80% pure) ... is 2-hydroxyethidium" (paragraph [00020] on page 4 of the application). To further clarify this, claim 1 has been amended accordingly. Further, the application in the same paragraph provides that "although 2-hydroxyethidium was inherently produced when HE-based prior art superoxide detection methods were practiced, 2-hydroxyethidium had never been substantially purified prior to the present invention[.]" further indicating that claims 1-5 are directed at subject matter obtained by a manmade process. There is no question to a skilled artisan as to what is "a 2-hydroxyethidium-

containing composition at least 80% (by weight) of which is 2-hydroxyethidium." Accordingly, applicants respectfully submit that claims 1-5 are definite.

The Examiner next rejected claims 6, 7, 9, and 10 as being incomplete for omitting essential elements which amounts to a gap between the elements. In particular, the Examiner alleged that a description of the detection protocol or means is not provided. While claims 6 and 7 recite a detecting step, applicants note that claims 9 and 10 recite a measuring step. Applicants respectfully traverse the rejection.

Claims 6, 7, 9, and 10 are method claims the elements of which are the steps recited in the claims. Applicants do not find any gap between the steps. MPEP § 2172.01 cited by the Examiner refer to two court cases: *In re Venezia*, 530 F.2d 956 (CCPA 1976) and *In re Collier*, 397 F.2d 1003 (CCPA 1968). However, these two cases do not support the rejection raised by the Examiner. *In re Venezia* is concerned with a kit claim in which interrelated parts may or may not be assembled to form a completed structure later. The CCPA held that what may or may not happen in the future is not part of the claimed invention and the claim satisfies the requirement of section 112, second paragraph. *In re Collier* is concerned with an apparatus claim in which the structural relationship between two elements of the apparatus is not positively recited. The CCPA held that the wording in the claim on intended uses, capabilities, and structure which will result upon performance of future acts cannot be considered as structural limitations and the claim is invalid for failing to meet the requirement of section 112, second paragraph. Unlike the claim in *In re Collier*, the steps recited in the claims at issue do not have any gap. A claim is not inherently indefinite just because it recites a detecting or measuring step. For example, a method claim (for testing whether an automatic home climate control system works) that involves the steps of (a) opening windows in a room, (b) detecting an increase or decrease in room temperature, and (c) observing the activation of an automatic home climate control system is clearly definite. Similarly, a method claim reciting the steps of (a) cutting a log to produce a rectangular wooden board and (b) measuring the length and width of the board is clearly definite. In the case of the instant application, a skilled artisan clearly recognizes that various methods are available for detecting the presence and/or measuring the amount of 2-hydroxyethidium and it is well within the capability of a skilled artisan use these methods. For example, in addition to the HPLC method illustrated in the application, other methods include electrospray MS, Fluorescence microscopy, thin layer chromatography, and element analysis. Therefore, there

will not be any question to a skilled artisan as to what the detecting/measuring step means. Accordingly, applicants respectfully submit that claims 6, 7, 9, and 10 are definite.

Anticipation rejection under 35 U.S.C. §102 (b)

The Examiner rejected claims 1-5 as being anticipated by Herlyn et al. (US 20020081711), alleging that Herlyn et al. disclosed 2-hydroxyethidium in section 0177. Applicants respectfully disagree.

First of all, Herlyn et al. recited the term "hydroxyethidium" in section 0177 and this does not constitute a disclosure of 2-hydroxyethidium because hydroxyethidium encompasses a genus of compounds that can have a hydroxyl group at various positions, not just position 2. As 2-hydroxyethidium is not specifically disclosed by Herlyn et al., claims 1-5 are not anticipated by Herlyn et al.

In addition, applicants respectfully submit that the hydroxyethidium recited in Herlyn et al. is in fact hydroethidine (also called dihydroethidium, see Zhao H et al. Free Radical Biology & Medicine 34:1359-1368, 2003, page 1359, left column) and Herlyn et al. made an typographical error to call the compound hydroxyethidium. This is supported by the following evidence. Herlyn et al. made it clear that the melanoma cell aggregation assay described therein was carried out as described in Degen et al. (Am. J. Pathol. 152:805-813, 1998, copy attached as Exhibit A). The abbreviation for the dye (HE), the amount of the dye used (40 micrograms per milliliter), and other experimental conditions such as the exposure time (60 minutes) described in Herlyn et al. (section [0177]) are exactly the same as those in Degen et al. (page 806, left column, lines 1-3 under "Reagents" and lines 7-9 under "Cell Aggregation Assay"). It is clear from Degen et al. that the fluorescent red dye used is hydroethidine (HE) obtained from Polysciences located in Warrington, PA (page 806, left column, lines 1-4 under "Reagents"). Applicants attach a copy of the technical data sheet for hydroethidine (Exhibit B) obtained from the Polysciences, Inc. webpage (<http://www.polysciences.com/shop/>). The data sheet indicates that Polysciences, Inc. is located in Warrington, PA and the molecular formula for hydroethidine is $C_{21}H_{21}N_3$, which matches that of hydroethidine but not 2-hydroxyethidium as provided in Fig. 1 of the present application. Nowhere in Degen et al. is the word hydroxyethidium mentioned. A search for "hydroxyethidim" in the Polysciences' online catalog did not return any match. A similar search for "hydroethidine" returned a match for the product for which the technical data

sheet is enclosed. In addition, the abbreviation HE used in Herlyn et al. is well recognized in the art as an abbreviation for hydroethidine. See, e.g., Macho A et al. Blood 86:2481-7, 1995 (abstract); Benov L et al. Free Radic Biol Med. 25:826-31, 1998 (abstract); Yagi Y et al. Cytometry 41:223-5, 2000 (abstract); Harvey RW et al. Appl Environ Microbiol 68:1872-81, 2002 (abstract); Zhao H et al. Free Radical Biology & Medicine 34:1359-1368, 2003 (abstract and left column on page 1359); Pyner S et al. Exp Physiol 88:733-40, 2003; and Papapostolou I et al. Anal Biochem 332:290-8, 2004 (abstract).

For the above reasons, applicants respectfully submit that claims 1-5 are not anticipated by Herlyn et al.

Anticipation rejection under 35 U.S.C. §102 (a) and obviousness rejection under 35 U.S.C. §103 (a) based on Zhao et al.

The Examiner rejected claims 1-25 under 35 U.S.C. §102(a) as being anticipated by, or alternatively under 35 U.S.C. §103(a) as being obvious over, Zhao et al. (Proc. Natl. Acad. Sci. US A 102:1359-1368, 2003). These two rejections are addressed separately below.

1. *Anticipation rejection under 35 U.S.C. §102 (a)*

As far as applicants can tell, Zhao et al. was published online on April 11, 2005 and on paper on April 19, 2005 and the present application was filed on April 8, 2004. Therefore, Zhao et al. was published within one year of the filing date of the present application. Applicants have attached a declaration (Exhibit C) by the two inventors explaining the discrepancy between the authorship of Zhao et al. and the inventorship of the present application and establishing that Zhao et al. disclosed applicants' own work. Applicant's disclosure of his or her own work within the year before the application filing date can not be used against him or her under 35 U.S.C. § 102(a). MPEP 2132.01 (citing *In re Katz*, 687 F.2d 450, 215 USPQ 14 (CCPA 1982)). Accordingly, withdraw of the rejection under 35 U.S.C. § 102(a) over Zhao et al. is respectfully requested in view of the declaration.

2. *Obviousness rejection under 35 U.S.C. §103 (a)*

To make a 35 U.S.C. § 103 rejection, the scope and content of prior art has to be determined. See *Graham v. John Deere*, 38 U.S. 1 (1966). "Before answering *Graham's* 'content' inquiry, it must be known whether a patent or publication is in the prior art under 35 U.S.C. § 102." *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1568 (Fed. Cir. 1987). As

discussed above, Zhao et al. was published within one year of the filing date of the present application and therefore it is not § 102(b) art. Also as discussed above, Zhao et al. does not qualify as prior art under § 102(a) because it is the applicants' own publication. Accordingly, withdraw of the rejection under 35 U.S.C. § 103(a) over Zhao et al. is respectfully requested.

Conclusion

Having addressed each rejection raised by the Examiner, the claims as amended are believed to be in condition for allowance and a Notice of Allowance is respectfully requested. Should any issues remain outstanding, the Examiner is invited to contact the undersigned at the telephone number appearing below if such would advance the prosecution of this application.

Respectfully submitted,



Zhibin Ren, Reg. No. 47,897
Quarles & Brady LLP
411 East Wisconsin Avenue
Milwaukee, WI 53202-4497
Phone (414) 277-5633
Fax (414) 271-3552

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